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EXAMINER	
CANELLA, KAREN A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,274	LEE ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8 and 11-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8 and 11-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/5/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Please note that the examiner assignment for this application has been changed.

Acknowledgement is made of applicant's election of Group VIII and the species of "breast cancer". After review and reconsideration of the instant claims in light of the prior art. both the Restriction Requirement and the Election of Species Requirement are withdrawn.

Claims 6, 7, 9 and 10 have been canceled. Claims 1, 4, 5, 8, 11, 13, 17 have been amended. Claims 39-42 have been added. Claims 1-5, 8, 11-42 are pending and under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 8, 11-19 and 39-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in the recitation of "small" molecule drug. The term "small" in claim 1 is a relative term which renders the claim indefinite. The term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 39 ad 40 are vague and indefinite in the recitation of "substantially similar" in structure. The term " substantially similar " in claims 39 and 40 is a relative term which renders the claims indefinite. The term " substantially similar " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Section 2173 of the M.P.E.P. states

Claims Must Particularly Point Out and Distinctly Claim the Invention

The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent..

In the instant case, the specification does not provide a limiting definition for a "small" molecule drug which would provide a boundary between that which is "small" versus that which is not small, or "medium". The specification does not provide a limiting definition for "substantially similar" which would serve to differentiate structures which were not substantially similar to either IBT13131 or IBT14664 or not. Thus, a potential infringer would not be able to ascertain when a drug molecule was large enough not to be considered small, or similar enough to be considered "substantially similar" and therefore outside the scope of the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8, 11-20 and 36-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of

direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988)..

(A) As drawn to the treatment of a human patient.

Claims 1-5, 9, 11-20 and 39-42 are drawn in part to a method for treating a disease involving cell hyperproliferation, including cancer and stenosis, comprising the administration of a small molecule drug which inhibits the interaction between Hec1 protein and at least one further protein. The specification provided a yeast two-hybrid screen to identify eight molecules that inhibit the interaction between Hec1 and Nek2 (page 40, lines 15-31) in yeast. The specification teaches that out of the eight molecules, only two molecules showed the ability to kill dividing HeLa cells (page 41, lines 8-28). The at teaches a number of cellular proteins in addition to nek2 that bind to Hec1, wherein the mutant phenotype of said proteins caused G2/M phase arrest (Clark et al, WO98/45433, page 46). Thus, the disclosure of inhibiting the interaction between Hec1 and Nek2 is not commensurate in scope with the inhibition of Hec1 and at least one further protein. Further, the toxicity of IBT13131 and IBT14664 on HeLa cells does not translate into a method of treating patients for cancer or for stenosis. The art recognizes that many compounds can show favorable activity in vitro but fail to show favorable activity in a clinical treatment. Mohanlal (WO0240717) teaches that an important reason for the high failure rate in clinical trials is the poor predictive value of currently used screening technologies for biological validation, pharmacological testing, and screening for success or failure of chemical entities and biologicals in clinical trials involving human subjects, which include screening based on in vitro assays, which inadequately represent the clinical disease phenotype of the patients in which the tested chemical entities or biologicals are intended to be used in the future. Mohanlal teaches that success of chemical entities or biologicals in cell screens does not necessarily translate into clinical success in patients because the majority of chemical entities or biologicals, while successful in said cell screens fail in clinical trials, particularly in late phase II and phase III trials for pharmacodynamic reasons (lack of efficacy and/or an unacceptable adverse event profile); and pharmacokinetic reasons. In the instant case, the specification teaches only toxicity toward Hela cells and Saos2 cells (page 42, lines 15-19) which provides not information on pharmacodynamics or pharmacokinetics. Further, claims 1-5, 9, 11-20 and 39-41 encompass diseased hyperprolific cells which are Rb positive as well as Rb

negative, but the specification teaches that IBT13131 is active against cells which are specifically Rb negative. the instant claims thus encompass Rb positive pathogenic cells which is not commensurate with the disclosure set forth.

(B) As drawn to prevention of a disease

Claims 1-5, 9, 11-20 and 39-42 are drawn in part to a method for preventing a disease involving cell hyperproliferation, including cancer and stenosis, comprising the administration of a small molecule drug which inhibits the interaction between Hec1 protein and at least one further protein. When given the broadest reasonable interpretation, "preventing" a disease involving cell hyperproliferation includes the prevention of such a disease before it occurs in a patient who has yet to experience said disease. The specification fails to teach how to identify patients who are about to develop the hyperproliferative disease; the specification fails to teach when to administer the small molecule drug before the disease occurs so as to prevent hyperproliferation. Thus, one of skill in the art would be subject to undue experimentation in order to use the instant methods for preventing a hyperproliferative disease.

(C) As drawn to molecules which are inactive in a mammalian cell.

Claim 37 is drawn in part to the molecules which had no activity on mammalian cells, such as IBT4282, IBT6432, IBT11830, IBT12008 and IBT15154 (page 41, lines 8-11).. The specification fails to teach an alternate use for said compounds beyond that of treating diseases involving cell hperproliferation. Thus, one of skill in the art would be subject to undue experimentation in order to find a use for said compounds.

(D) As drawn to molecules which have yet to be identified, molecules which are not known in the art and molecules having substantially similar structures to IBT13131 and IBT14664.

Claim 36 is drawn to a molecule or ligand identified by the method of clam 21 wherein said molecule of ligand lessens proliferation when contacted with proliferating cells. claim 38 is drawn to a composition comprising the molecule or ligand of claim 36 and a pharmaceutically acceptable carrier. Claim 21 is an assay for identifying a compound that reduces the interaction between Hec1 and at least one further protein. The specification has taught only two molecules, IBT13131 and IBT14664 which reduce inhibit the interaction between Hec1 and Nek2 and inhibit the proliferation of mammalian cells, specifically RB deficient mammalian cells. The art teaches a number of cellular proteins in addition to nek2 that bind to Hec1, including Rb,

wherein a dominant-negative Hec1 mutant consisting of a long series of Leu heptad repeats caused G2/M phase arrest (Clark et al, WO98/45433, page 4, lines 5-7 and lines 16-20 and page 46). Thus the claims are again not commensurate in scope with the disclosure which specifically teaches the inhibition of the Hec1 and Nek2 interaction, rather than the broadly claimed Hec1 and "a further protein". The specification teaches that the two molecules, IBT13131 and IBT14664, are related by possession of a phenyl-thiozole benzamide structure. the specification teaches no alternative core structures necessary for the inhibition of binding between Hec1 and a "further protein", or Hec1 and Nek2. Thus, the specification fails to enable the scope of a "molecule or ligand" of claims 36 and 38. Further, claims 40 and 41 encompass variants of IBT13131 and IBT14664. Although the specification states that the compounds, IBT13131 and IBT14664, are related by possession of a core pheynl-thiozol-benzamine structure, the specification has failed to provide objective evidence that said core structure is the minimal structure requires for inhibition of the Hec1-Nek2 interaction. Thus one of skill in the art would be forced to determine the tolerance of variants of IBT13131 or IBT14664 to structural modifications with regard to the ability of said compounds to disrupt the interaction between Hec1 and Nek2 and cause cell death on Rb negative mammalian cells.

In order to conform to 112, first paragraph, it is necessary for the specification to teach how to make the molecules and ligands of the invention. It is noted that claims 36 and 38 encompass molecules which have yet to be identified, therefore one of skill in the art would be forced into both the identification of said compounds as well as determining how to make said compounds. With regard to the two active compounds of claim 36, it is noted that IBT14664 is currently known in the art as portion of a "chemical mix" (ChemDB, page 1 of 3, downloaded from the Web on February 9, 2009). However, it is unclear if said compound, and means to isolate or synthesize said compound, were known in the art at the time the instant priority application was filed. Further, IBT 13131 appears not to be known in the art. The specification does not provide instruction or guidance for how to make any of the compounds of claim 37 or the variants of claims 40 and 41. The art teaches that organic synthesis of a multifunctional molecule is not trivial undertaking. The art teaches that presence of differing functional groups, heteroatoms and three dimensional configurations require different considerations as to protecting groups, and reactivity manifest in different synthetic strategies (Sierra and de la Torre,

Angewandte Chemie, 2000, Vol. 39, pp. 1538-1559, especially pages 1544-1546, "Troublesome Protecting Groups"). Chemical structure heterogeneity including the presence of different heteroatoms on different three dimensional structures can radically alter the reactivity of any other atom within a molecule through inductive effects (page 1545, second column, lines 2-6 of the second full paragraph and lines 4-7 of the third full paragraph, resonance effects, acidity, basicity and steric hindrance (page 1552-1554), strain (page 1554-1557) or transition state crowding (page 1545, second column, second full paragraph, lines 2-6,, page 1546, second column, first full paragraph) and therefore can radically influence the reactivity with any given reagent contacted thereto. sierra and de la Torre teach that a well-testing transformation can fail for complex reasons (Sierra and de la Torre, ibid, page 1540, first column, lines 9-11, page 1541, first column, lines 33-37, under the heading "Working Models that do not Work", page 1542, first column, lines 15-17, even when supported by molecular mechanics calculations (page 1542, first column, lines 6-9) and what is seen as an innocuous alteration can cause a failure in a synthetic step (page 1542, second column, lines 9-12). Sierra and de la Torre teach that the presence of remote substitutions has unexpected influence over a chemical step (pages 1546-1548, under the heading "The Unexpected Influence of Remote Substituents") Sierra and de la Torre state that "As the complexity of intermediates increases, the number of variables involved in a simple transformation grow exponentially making predictions about the outcome of any given synthetic step on a highly functionalized intermediate, unreliable (page 1548, second column, lines 5-8 of the second full paragraph, page 1550, second column, lines 1-9 under the heading "The Trivial Functional Group Transformation"). Sierra and de la Torre conclude that the lack of predictability in so many cases and the very empirical nature of synthetic organic chemistry implies that the science is not fully developed (page 1548, second column, lines 13-16 of the second full paragraph). Sierra and de la Torre state that alternate routes can then be devised which circumvent a failed transformation (page1548, second column, lines 10-13 of the second full paragraph), however, the sum total effort of designing and redesigning represents undue experimentation to one of skill in the art, exemplified by Sierra and de la Torre as "the amount of effort devoted to simple transformations is still quite enormous" (page 1557, first column, lines 15-18). It is noted that the inhibitor of Hec1-Nek2 interaction as claimed in claim 37 are all densely functionalized molecules. The specification provides no means of making said

compounds. Thus, one of skill in the art would be subject to undue experimentation in order to make the compounds disclosed by the instant application.

Given the lack of teachings and guidance provided by the instant application for all the reasons above. one of skill in the art would be subject to undue experimentation in order to carry out the claimed methods and make the claimed molecules or ligands.

Claims 1-5, 8, 11-20, 36 and 38-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claims 36 and 38 encompass molecules or ligands which are not limited to the IBT series of molecules in claim 37. The description of the IBT series of compounds fails to adequately describe the genus of molecules encompassed by the claim because the genus is not limited by structures which are similar to the IBT series. The genus is in fact characterized only by function, that of being identified by the method of claim 21 and therefore commensurate with inhibiting the interaction between Hec1 and "at least one further protein". Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art

therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. In the instant case, a compound identified by the method of claim 21 will be a compound which inhibits the interaction between hEc1 and "at east one further protein" and is thus an indicator of what the molecule does rather than what it is. Further, one cannot describe what one has not yet conceived (Fiddes v Baird, 30 USP2d 1481 at 1483. The description of the molecules listed in claim 37 fails to adequately describe the genus of compounds encompassed by the claims because the genus includes compounds which inhibit the interaction between Hec1 and proteins other than Nek2. One of skill in the art would reasonably conclude that applicant was not in possession of the claimed genus at the time of filing.

Claims 40 and 41 encompass small molecule drugs which are substantially similar to IBT13131 and IBT14664. The description of IBT13131 and IBT14664 fails to adequately describe the genus of molecules which are substantially similar to IBT13131 and IBT14664 because the specification fails to adequately correlate the structure of IBT13131 and IBT14664 to the ability to inhibit the interaction of Hec1 and Nek2. The specification suggests but does not demonstrate that the phenyl-thiozol-benzamide structures the core structure, but there are not teachings in the specification that this proposed core structure is a minimal structure adequate to carry out the inhibition of binding between Hec1 and Nek2. Upon confronted with a molecule possessing the "core structure" it would be necessary to first empirically test said molecule for inhibition of interaction between Hec1 and Nek2 and subsequent inclusion into the genus of "small molecule drugs". Therefore it is concluded that thus, the specification fails to adequately describe the genus of molecules encompassed by claims 36 and 38-41. It logically follows that the methods claims 1-5, 8, 11-20, and 39-42, which are dependent upon the identity of the small molecule drugs, are also not adequately described.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21, 22, 26, 28, 29, 32, 33, 35 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Clark et al (WO98/45433).

Claim 21 is drawn to a method comprising the steps of contacting Hec1 protein and at least one further protein in the absence and presence of the compound and determining the relative amount of interaction between the Hec1 protein and the at least one further protein. Claims 22 embodies the method of claim 21 wherein the at least one further protein is Nek2. Claim 26 embodies the method of claim 21 wherein the contacting in the presence and absence of the compound is done by immunoprecipitation.

Claim 28 is drawn in part to a method comprising the steps of contacting a sample comprising cells with a molecule or a combination of molecules and measuring the amount of cell cycle proliferation and arrest. Claim 29 embodies the method of claim 28 wherein the sample comprises isolated cells

Claim 32 is drawn to a method comprising the steps of synthesizing a potential ligand, contacting said potential ligand with a Hec1 protein domain containing protein and determining whether the potential ligand binds to the Hec1 protein domain containing protein. Claim 33 embodies the method of claim 32, further comprising determining whether the ligand reduced cell proliferation. Claim 35 embodies the method of claim 32 wherein the potential ligand is designed from a known compound.

Claim 36 is drawn to a molecule or ligand identified by the method of claim 21.

Clark et al disclose a method comprising the steps of making an anti-Hec1 antibody which fulfills the requirements of "designing a ligand" and "designed from a known compound" of claims 32 and 35. Clark et al disclose that hybridomas which produced anti-Hec antibodies can be screened by Elisa and Western Blot (page 10, lines 35 and lines 8-9) which fulfills the specific embodiment of claim 32 part c, of determining whether the ligand binds to the Hec1 protein domain containing protein. Clark et al disclose that injection of the anti-Hec1 antibody

into cells does not arrest cells in mitosis but allows said cells to proceed aberrantly (page 15,, lines 16-18), which fulfills the specific embodiment of claim 33 requiring a determination of whether the ligand reduces cell proliferation. It is noted that Clark teaches the negative, that the antibody does not reduce cell proliferation, but the act of determining as taught by Clark et al fulfills the requirement of claim 33.

Clark et al disclose a method wherein transfection of cells with a Hec mutant protein containing only the long series of leucine heptad repeats and to interact through said repeats with several protein important for mitosis including Nek2, sb1.8 and two different regulator subunits of the 26S proteasome, MSS! and p45 (page 4, lines 17-22).. Clark et al disclose that the in vivo binding of the mutant Hec protein and the interacting proteins was determining by reciprocal co-immunoprecipitation (page 46, Table 3) which fulfills the limitations of claims 21, 22, 26 and 36. Clark et al disclose that the transfection of the dominant negative Hec1 protein caused G2/M arrest (page 46, Table 3) which meets the specific embodiment of claims 28 and 29 with regard to cell cycle progression and arrest.

Claims 28, 30 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Zimmermann et al (U.S. 5,516,775).

Claim 30 embodies the method of claim 28 wherein the sample is a tissue sample. claim 31 specifies that the tissue sample is in an organism.

Zimmermann et al discloses a method wherein a piece of human T24 bladder carcinoma is transplanted into nude mice followed by the administration to the mice of a compound of formula I or a placebo (column 6, line 60 to column 7, line 10). Zimmermann et al disclose the measurement of tumor volume (column 7, lines 11-21), which is commensurate with the measurement of an amount of cell proliferation.

It is noted that the recitation of a "method for identifying a molecule that interferes with a function of Hec1 protein, Nek2 protein and/or Hint1 protein and inhibits cell proliferation" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone.

See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

It is further noted that the phrase "wherein by a decrease in cell proliferation, a decrease in cell cycle progression, an increase in cell cycle arrest, or an increase in apoptosis in the sample comprising proliferating cells exposed to the molecule or combination of molecules, relative to the amount of proliferation, cell cycle progression, cell cycle arrest, or apoptosis in a sample comprising proliferating cells mot contacted with the molecule or combination of molecules, identifies a molecule or combination of molecules that inhibit proliferation of the cells" is not given patentable weight when comparing the claims to the prior art as it simply expresses the intended result of a process step positively recited, see MPEP 2111.04.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21, 22, 24, 25, 28, 29, 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al (WO98/45433) in view of Chumakov et al (WO 03/050281).

Claim 24 embodies the method of claim 21 wherein the Hec1protein is immobilized. Claim 25 embodies the method of claim 21 wherein the at least one further protein is immobilized.

Claim 34 embodies the method of claim 32 wherein the potential ligand is designed de novo. Claim 35 embodies the method of claim 32 wherein the potential ligand is designed from a know compound.

Clark et al teach that the Hec protein is encoded by the Hec gene which is highly expressed in cancer, and that Hec interacts through leucine heptad repeats with several proteins involved in mitosis, including nek2, ab1.8 and two different regulatory subunits of the 26S proteosome, MSS1 and p45. Clark et al suggest that the biochemical properties of HEC indicate a potential role in modulating proteins important of mitosis and M phase progression (abstract). Clark et al teach that HEC may function as an adaptor molecule through the long leucine heptad repeats (page 4, lines 23-24). Clark et al teach that an understanding of the molecular events of mitosis will lead to the identification and development of agents to control cell proliferation (page 3, lines 28-30). Clark et al do not specifically teach the screening of non-Hec1 mutant molecules by ELISA to identify agents which interfere with the ability of Hec to bind to nek2, ab1.8 MSS1 and p45.

Chumakov et al teach that the screening by ELISA for one or more antagonists which block the binding between two polypeptides is well known in the art (page 84, line 36 to page 85, line 1).

It would have been prima facie obvious at the time that the claimed invention was made to use an ELISA assay wherein either the Hec1 protein is immobilized, or the Nek2 protein is immobilized to screen for agents which block or reduce the binding to Hec1 to Nek2. One of skill in the art would have been motivated to do so by the suggestion of Clark et al that Hec1 interacts with Nek2 which is important in mitosis and that agents can be developed to control cell proliferation, in addition to the teachings of Chumakov et al that the ELISA screening for antagonists to a protein-protein interaction is well known in the art.

Claims 21, 22, 27-29, 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al (WO98/45433) in view of Burgessi et al (U.S. 6,613,531).

Claim 27 embodies the method of claim 21 which includes co-localization of labels specific for the Hec1 protein and the further protein.

Clark et al teach that the Hec protein is encoded by the Hec gene which is highly expressed in cancer, and that Hec interacts through leucine heptad repeats with several proteins involved in mitosis, including nek2, ab1.8 and two different regulatory subunits of the 26S proteosome, MSS1 and p45. Clark et al suggest that the biochemical properties of HEC indicate a potential role in modulating proteins important of mitosis and M phase progression (abstract). Clark et al teach that HEC may function as an adaptor molecule through the long leucine heptad repeats (page 4, lines 23-24). Clark et al teach that an understanding of the molecular events of mitosis will lead to the identification and development of agents to control cell proliferation (page 3, lines 28-30). Clark et al do not specifically teach the screening of non-Hec1 mutant molecules by co-localization of labels to identify agents which interfere with the ability of Hec to bind to nek2, ab1.8 MSS1 and p45.

Burgess et al teach a method wherein an agent which inhibits the binding of a subunit to a polymerase can be identified by determining the proximity of a first label for the subunit and the second label for the polymerase, the first and second labels being different (claims 3 and 4).

It would have been prima facie obvious at the time the claimed invention was made to label Hec1 and Nek2 wit different labels and use the labeled substrates in a method for identifying an inhibitor of the binding of Nek2 to Hec1. One of skill in the art would have been motivated to do so by the suggestion of Clark et al that Hec1 interacts with Nek2 which is important in mitosis and that agents can be developed to control cell proliferation, in addition to the teachings of Burgess et al on the use of dual labels for two parts of a protein complex in a method of screening for an inhibitor for the association of the two parts of said complex.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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